



Influenza vaccination dilemmas

Zarema Obradović^{1,2*}, Amina Obradović¹, Arzija Pašalić²

¹Institute for Public Health of Canton Sarajevo, Sarajevo Bosnia and Herzegovina, ²Faculty of Health Studies, University of Sarajevo, Sarajevo, Bosnia and Herzegovina

ABSTRACT

Influenza is one of the most common respiratory diseases in the world, annually causing over one million of deaths. It is triggered by one of the influenza viruses (A, B, or C). In most cases, it occurs in epidemic form, but it can also appear in pandemic form, and very occasionally, it occurs in sporadic form. In the temperate zones, influenza occurs during the winter months of a year. In the tropics, however, it occurs throughout the year, although the highest number of patients is registered during the rainy seasons. In young and otherwise healthy individuals influenza is a mild disease; however, if affecting individuals with a weakened immune system, it can lead to health complications and even to death. The only effective preventive measure to preclude the disease is vaccination. There is still no consensus on whether the vaccination should be compulsory or recommended and which population groups should be vaccinated. In most European countries, the vaccination is recommended for some population groups, while in the United States the vaccination is recommend to all individuals above six months of age.

Keywords: Influenza; vaccination; dilemmas

INTRODUCTION

Acute respiratory infections are the most common infections in the world. They cause significant morbidity and mortality, particularly in elderly people and pregnant women with history of health problems. A significant increase in overall mortality was registered in the countries of the Northern hemisphere during the 2014-2015 winter season. In Italy, for example, this increase amounted to +13% and was directly associated with influenza virus circulation (1).

Acute respiratory infections are caused by different types of microorganisms. Most commonly, they are associated with influenza type A and B, and less commonly with influenza C virus. Thus, influenza (also known as the flu) is considered to be one of the most common acute respiratory infections. Each year, the flu causes over one million of deaths worldwide (2).

The pandemic influenza viruses have an exceptionally high impact on morbidity and mortality, as it was demonstrated in 2009, when the influenza A subtype H1N1 led to a pandemic, causing the death of 18,449 people in only one month of that year (3).

Influenza viruses are constantly circulating, but their concentration in open space is never that high to get infected when spending time outside. The outbreak of influenza is more commonly associated

*Corresponding author: Zarema Obradovic, Institute for Public Health of Canton Sarajevo, Sarajevo, Bosnia and Herzegovina. E-mail: zobradovic9@gmail.com

Submitted: 10 October 2016/Accepted: 14 November 2016

DOI: <http://dx.doi.org/10.17532/jhsci.2016.398>



with indoor spaces due to the presence of a larger number of people at one place, including individuals with the flu. Related to that is the fact that in the temperate zones, influenza is a seasonal disease, occurring during cold or winter seasons, when humidity and temperature are low, and people have to spend most of the time indoor (4,5). The highest rate of the infection occurs in the period between January and April (6). In tropical areas, where the virus circulation varies little throughout the year, the highest number of patients is registered during the rainy seasons.

Usually, a large number of people is affected by influenza at the same time, thus the epidemic form is more common than the sporadic form. The occurrence of the disease is determined by environmental and social factors. The most important environmental factors are outdoor temperature and humidity, while social factors include equality in health care system, availability of vaccine, and the age of population. These factors play a major role in occurrence and spread of influenza (7).

Seasonal influenza causes a significant burden to public health system due to a large number of affected people who cannot effectively perform their daily tasks and contribute to the society. At the same time, these patients spend more money to purchase the analgesics, antipyretics, and food rich in vitamins compared with healthy people.

INFLUENZA CHARACTERISTICS

Although everyone can be affected by influenza regardless of gender and age, various epidemics and pandemics occur differently within certain age groups. For example, during the pandemic influenza that occurred in 2009, the largest number of patients were in the age group between 21 and 30 years.

Influenza begins with general infectious syndrome (general weakness, fatigue, fever, pain in the bones and joints) and continues with symptoms of respiratory tract infection (sneezing, coughing, runny nose, and watery eyes).

At the beginning of epidemics, the disease is hard to diagnose due to the sporadic form of influenza, and laboratory testing is required. Polymerase chain reaction (PCR) is the best method for virus

identification. In addition, to determine the diagnosis, it is very important to have the epidemiological data on co-occurrence of similar diseases in the patient's environment, as well as to have data on the movement of influenza during the same period in several previous years.

Respiratory diseases caused by respiratory syncytial virus (RSV), which frequently affects young children (8), often pose diagnostic problems when diagnosing influenza.

Although, the clinical picture is mild in most cases and the disease ends in patient's healing, in some cases, influenza can cause various complications. These complications are common in individuals with a weakened immune system, such as elderly people and patients with chronic diseases [e.g., heart and vascular diseases, chronic lung diseases, uncontrolled diabetes mellitus, and oncological diseases] (9). The flu can also be a serious disease for pregnant women because they are at increased risk of developing complications compared with other individuals of the same age (10).

In general, the most common influenza complications are pneumonia, otitis media, inflammation of the heart muscle, and deterioration of the underlying (already existing) illness. In the most severe cases, the flu can also lead to death (11).

INFLUENZA VACCINATION

It is generally accepted that vaccination is the only effective preventive measure against influenza. Moreover, vaccination is especially important when the influenza is caused by the viruses with pandemic potential, where it is used to prevent or at least to control pandemic influenza (12).

A number of studies investigated an optimal vaccination strategy against influenza viruses, which includes the need for vaccination, sufficient quantities of the influenza vaccine, and satisfactory vaccination coverage. An important segment of the vaccination policy is related to the time frame for the implementation of the vaccination program (13).

Several dilemmas related to the influenza vaccination exists, and the two major are:

1. Whether influenza vaccination should be a recommended or compulsory activity; and
2. Who should be vaccinated against influenza?

Each country has different approach in determining whether the vaccination against influenza should be recommended or compulsory, to prevent and control seasonal influenza in those areas. In most countries, the vaccination against seasonal influenza is recommended. Similarly, different countries have different recommendations for selecting the target groups for influenza vaccination.

Recently, European countries considered to make the influenza vaccination compulsory. Children aged from 2 to 17 years are proposed as the target group. It is assumed that this strategy would directly reduce the morbidity in this age group, and, indirectly, it would reduce the morbidity in adults as well, considering that 1/3 of all adult diseases are prevented in this way (14).

In 2011, the European Union (EU) introduced the live attenuated influenza vaccine (LAIV) for healthy children and adolescents aged 2-17 years. The vaccine is applied intranasally. Simulation studies conducted in Germany indicated that the vaccination of this age group would lead to a significant reduction in overall morbidity and have a positive economic effect on health insurance (15,16).

For the 2015/16 influenza season, the United States (US) recommended routine annual influenza vaccination for all individuals above 6 months of age without contraindications (17). One of the main arguments for this recommendation is reducing the burden to society caused by the flu each year.

A survey conducted in the US showed that an average influenza season results in over 30,000 people diagnosed with the flu and over 3,500 hospitalized patients, directly or indirectly, leading to death in over 720 patients. On the other hand, it has been proved that the vaccination significantly reduces the morbidity and mortality in the US (18).

Target groups for influenza vaccination

Due to frequently reported positive effects of the influenza vaccination on morbidity and mortality reduction in different parts of the world, a number of manuals and guidelines on vaccination have been developed. Thus, the European guide focuses on the vaccination of particularly vulnerable population groups such as individuals over 65 years of age, those with a weakened immune system, pregnant women,

and health care workers. Adequate vaccination coverage of these groups would significantly reduce the burden caused by influenza (1). Nevertheless, the influenza vaccination coverage in Europe is still relatively low, even when observed per individual risk groups (19).

Vaccination of elderly people

One of the most vulnerable groups affected by influenza are people aged 65 years and more. It is considered that such individuals have weakened immunity, and often suffer from chronic diseases that can be significantly worsened by influenza. According to a survey conducted in 2008 in European countries, the vaccination coverage of individuals over 65 years old differed considerably from one part of Europe to another, and ranged from 2 to 80%. The lowest coverage was recorded in Poland. One of the explanations for the low vaccination coverage was that the vaccine was not provided free of charge (19).

When considering elderly population, the risk of influenza is particularly high in the group accommodated in nursing homes, so the vaccination coverage should be a priority in this group. Influenza vaccination of elderly people would also prevent 50-68% of pneumonia cases, as this is one of the most common complications of influenza in this population group. When the influenza vaccination is not administered in time, outbreak of influenza epidemics in nursing homes is treated by antiretroviral therapy given within 12 to 48 hours. When compared to the vaccination, such treatment is considerably more complicated for the patients, and more expensive for the health care system (20).

Vaccination of individuals with a weakened immune system and chronic diseases

Influenza is considered a mild disease for individuals with a healthy immune system, but it can be very serious for immunocompromised individuals, and those with chronic diseases. Therefore, such individuals are in the group recommended for the influenza vaccination. This group also includes HIV-positive people who need to be vaccinated by an inactivated vaccine because the live vaccine could further damage their health. To achieve an adequate

immune response, the vaccination should be carried out while the patient's immune system is still strong (21).

Since the influenza has a negative impact on various chronic diseases, especially chronic respiratory and cardiovascular diseases, and can worsen the underlying disease condition, the patients suffering from such diseases should also be vaccinated against influenza (22,23).

Influenza vaccination of pregnant women

Influenza vaccination of pregnant women is conducted to protect pregnant women and mothers, as influenza is more likely to cause severe illness in this population group. Pregnant women show a high sensitivity to some types of the influenza viruses that can even lead to their death. At the same time, the vaccination of pregnant women also ensures the protection of fetus during the pregnancy as well as the protection of newborn babies during the period when the vaccine-preventable diseases, including the flu, have a significant impact on morbidity and mortality in this age group. The inactive vaccine against influenza is recommended for pregnant women. If the vaccination is not carried out during the pregnancy, it is recommended to be vaccinated after the delivery, to protect a newborn child (24,25).

All available data on the effects of vaccination on pregnant women and mothers show significant benefits for both, a mother and child. Therefore, it is necessary to conduct more effective social campaigns as well as to involve more actively gynecologists and midwives in promoting the vaccination of pregnant women (26).

Influenza vaccination of health care workers

In terms of influenza vaccination, health care workers are a particularly important population group to consider, for several reasons. Their daily contact with patients puts them at a higher risk of getting the flu compared with general population. Moreover, infected health care workers can easily spread the disease, especially to vulnerable groups of patients, in which influenza may worsen their pre-existing medical conditions, and even cause death. Since the 70s of the last century, the transmission of influenza viruses in health care institutions has been

documented, even in the form of intrahospital epidemics (27). In addition, health care workers can also transmit the flu to their family members (28). Nevertheless, not all groups of health care workers are equally important to be considered for influenza vaccination. For ethical reasons, it is recommended to make the vaccination compulsory for health care professionals who work with high risk categories of patients [e.g., premature infants, neonates, the elderly, individuals with immune deficiencies and chronic diseases] (29). Although the recommendations for annual vaccination of health care workers were issued back in 1984, the vaccination coverage has not yet achieved a satisfactory level (30).

A study conducted in France, in 102 centers for accommodation and treatment of elderly people, pointed out the challenges of the influenza vaccination of health care personnel. The study showed lack of motivation and knowledge of health care workers about the vaccine and influenza vaccination programs. In addition, the organizational issues contributed to low vaccination coverage (31). According to the research of Kramarz et al. (32), the influenza vaccination coverage is relatively low and rarely reaches 40% (32).

Health care professionals employed in care homes for elderly people are also at a high risk of getting influenza, so their vaccination is an important measure for the suppression of severe forms of influenza and nosocomial outbreaks in geriatric centers. A group of French authors analyzed published articles on geriatrics, infectious diseases, pneumology, and vaccination. Their results showed a lack of influenza vaccination coverage of workers employed in geriatric units. The lowest vaccination coverage was identified among young non-health care female workers (33).

Health care workers should undergo influenza vaccination for their own protection, protection of their families, and patients with whom they work. Among the factors that influence the decision to refuse vaccination are: the fear of vaccines, fear of adverse reactions, distrust in the effectiveness of vaccination, inadequate understanding of the impact of vaccination on health or disease. Related to this are also problems with the organization of the vaccination program (32).

A number of health care authorities recommend routine influenza vaccination for health care workers. This was particularly important during a pandemic occurrence of influenza A H1N1 in 2009, when the World Health Organization (WHO) recommended the influenza vaccination for all health care workers. In addition the immunization reduces the absence of health care workers from work, which has positive effects on economy as well.

Currently, 88% of countries recommend the vaccination of health care workers, and 61% also provides the financial support for the process. There is a positive trend in increasing the number of vaccinated health care workers as a result of education on the importance of vaccination, and its easier accessibility and availability (2).

According to the results of studies conducted between 1985 and 2002, the vaccination coverage of health care workers ranged from 2.1 to 82%. Vaccination campaigns included both training of health care workers and easier access to vaccines. The two main reported obstacles were: inadequate influenza risk assessments and underestimation of a risk to transmit the disease to patients. It is therefore important to make a vaccination campaign adapted to the specific requirements of each health care institution (34).

Vaccination of health care workers in a Saudi hospital in the 2008-2009 season was relatively low and covered 34.4% of the health care personnel. Ninety-five percent of the workers agreed to vaccination for their own protection, while doubts on the effectiveness of the vaccine in preventing the disease were the main reason in the worker group who refused to be vaccinated (35).

CONCLUSION

Influenza is an acute respiratory disease, which annually affects a large number of people. Influenza is a mild disease in young, otherwise healthy people. However, it can cause severe complications and even death in patients suffering from chronic diseases or with low immunity. Vaccination is the best preventive measure to suppress the influenza virus, but the dilemma whether to make this vaccination compulsory or recommended and which groups should be subjected to vaccination have not been resolved yet.

Based on their experience, many countries reported that influenza vaccination should be compulsory for the following groups: people over 65 years of age, individuals with weakened immune system, pregnant women, and health care workers. The vaccination of these population groups would significantly reduce their morbidity and mortality rates, and at the same time, bring considerable financial savings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Constatino C, Vitale F. Influenza vaccination in high risk groups: A revision of existing guidelines and rationale for an evidence-based preventive strategy. *J Prev Med Hyg* 2016;57(1): E13-8.
2. Music T. Protecting patients, protecting healthcare workers: A review of the role of influenza vaccination. *Int Nurs Rev* 2012;59(2):161-7. <https://doi.org/10.1111/j.1466-7657.2011.00961.x>.
3. Saxena S, Singh D, Zia A, Umrao J, Srivastava N, Pandey A, et al. Clinical characterization of influenza A and human respiratory syncytial virus among patients with influenza like illness. *J Med Virol* 2007;89(1):49-54. <https://doi.org/10.1002/jmv.24607>.
4. Tamerius JD, Shaman J, Alonso WJ, Bloom-Feshbach K, Uejio CK, Comrie A, et al. Environmental predictors of seasonal influenza epidemics across temperate and tropical climates. *PLoS Pathog* 2013;9(3):e1003194. DOI: 10.1371/journal.ppat.1003194.
5. Deyle ER, Maher MC, Hernandez RD, Basu S, Sugihara G. Global environmental drivers of influenza. *Proc Natl Acad Sci USA* 2016;113(46):13081-6. DOI: 10.1073/pnas.1607747113.
6. Goktas S, Sirin MC. Prevalence and seasonal distribution of respiratory viruses during the 2014-2015 season in Istanbul. *Jundishapur J Microbiol* 2016;9(9):e39123.
7. Sooryanarain H, Elankumaran S. Environmental role in influenza virus outbreaks. *Annu Rev Anim Biosci* 2015;3:347-73. <https://doi.org/10.1146/annurev-animal-022114-111017>.
8. Fleming DM. Influenza diagnosis and treatment: A view from clinical practice. *Philos Trans R Soc Lond B Biol Sci* 2001;356(1416):1933-43. <https://doi.org/10.1098/rstb.2001.1008>.
9. Hermann B, Lehnert N, Brodhun M, Boden K, Hochhaus A, Kochanek M, et al. Influenza virus infections in patients with malignancies - characteristics and outcome of the season 2014/15. A survey conducted by the Infectious Diseases Working Party (AGIHO) of the German Society of Haematology and Medical Oncology (DGHO). *Eur J Clin Microbiol Infect Dis* 2016 Nov 12 [Epub ahead of print]. <https://doi.org/10.1007/s10096-016-2833-3>.
10. Divala TH, Kalliani-Phiri L, Mawindo P, Nyirenda O, Kapito-Tembo A, Laufer MK. Incidence and seasonality of influenza-like illnesses among pregnant women in Blantyre, Malawi. *Am J Trop Med Hyg* 2016;95(4):915-17. <https://doi.org/10.4269/ajtmh.16-0243>.
11. Grohskopf LA, Sokolow LZ, Broder KR, Olsen SJ, Karron RA, Jernigan DB, et al. Prevention and control of seasonal influenza with vaccines. *MMWR Recomm Rep* 2016;65(5):1-54. <https://doi.org/10.15585/mmwr.r6505a1>.

12. Ghendon Y. Influenza vaccines: A main problem in control of pandemics. *Eur J Epidemiol* 1994;10(4):485-6.
<https://doi.org/10.1007/BF01719683>.
13. Jaberī-Douraki M, Moghadas SM. Optimal control of vaccination dynamics during an influenza epidemic. *Math Biosci Eng* 2014;11(5):1045-63.
<https://doi.org/10.3934/mbe.2014.11.1045>.
14. Rose MA, Damm O, Greiner W, Knuf M, Wutzler P, Liese JG, et al. The epidemiological impact of childhood influenza vaccination using live-attenuated influenza vaccine (LAV) in Germany: predictions of a simulation study. *BMC Infect Dis* 2014;14:40.
15. Damm O, Eichner M, Rose MA, Knuf M, Wutzler P, Liese JG, et al. Public health impact and cost-effectiveness of intranasal live attenuated influenza vaccination of children in Germany. *Eur J Health Econ* 2015;16(5):471-88.
<https://doi.org/10.1007/s10198-014-0586-4>.
16. Lee S, Chowell G. Exploring optimal control strategies in seasonally varying flu-like epidemics. *J Theor Biol* 2016;412:36-47.
<https://doi.org/10.1016/j.jtbi.2016.09.023>.
17. Clements KM, Meier G, McGarry LJ, Pruttivarasin N, Misurski DA. Cost-effectiveness analysis of universal influenza vaccination with quadrivalent inactivated vaccine in the United States. *Hum Vaccin Immunother* 2014;10(5):1171-80.
<https://doi.org/10.4161/hv.28221>.
18. Monto AS. Seasonal influenza and vaccination coverage. *Vaccine* 2010;28(Suppl 4):D33-44.
DOI: 10.1016/j.vaccine.2010.08.027.
19. Kramatz P, Ciancio B, Nicoll A. Seasonal and pandemic influenza vaccines for elderly and other risk groups: A review of available data. *Pol Arch Med Wewn* 2009;119(10):654-9.
20. Drink PJ. Influenza vaccination and antiviral therapy: Is there a role for concurrent administration in the institutionalized elderly? *Drugs Aging* 2003;20(3):165-74. <https://doi.org/10.2165/00002512-200320030-00001>.
21. Pancharoen C, Ananworanich J, Thisyakorn U. Immunization for persons infected with human immunodeficiency virus. *Curr HIV Res* 2004;2(4):293-9.
<https://doi.org/10.2174/1570162043351084>.
22. Trogdon JG, Nurmagambetov TA, Thomson HF. The economic implications of influenza vaccination for adults with asthma. *Am J Prev Med* 2010;39(5):403-10.
<https://doi.org/10.1016/j.amepre.2010.07.012>.
23. Jiang Y, Zhang Y. Association of influenza, influenza vaccination and cardiovascular risk. [Article in Chinese]. *Zhonghua Yu Fang Yi Xue Za Zhi* 2016;50(2):110-3.
DOI: 10.3760/cma.j.issn.0253-9624.2016.02.002.
24. Munoz FM. Maternal immunization: An update for pediatricians. *Pediatr Ann* 2013;42(8):153-8.
<https://doi.org/10.3928/00904481-20130723-09>.
25. Keller-Stanislawski B, Englund JA, Kang G, Mangtani P, Neuzil P, Nohynek H, et al. Safety of immunization during pregnancy: A review of the evidence of selected inactivated and live attenuated vaccines. *Vaccine* 2014;32(52):7057-64.
<https://doi.org/10.1016/j.vaccine.2014.09.052>.
26. de Martino M. Dismantling the taboo against vaccines in pregnancy. *Int J Mol Sci* 2016;17(6). pii: E894.
<https://doi.org/10.3390/ijms17060894>.
27. Stewart AM, Cox MA. State law and influenza vaccination of health care personnel. *Vaccine* 2013;31(5):827-32.
<https://doi.org/10.1016/j.vaccine.2012.11.063>.
28. Galanakis E, Jansen A, Lopalco PL, Giesecke J. Ethics of mandatory vaccination for healthcare workers. *Euro Surveill* 2013;18(45):20627.
<https://doi.org/10.2807/1560-7917.ES2013.18.45.20627>.
29. Simeonsson K, Summers-Bean C, Connolly A. Influenza vaccination of healthcare workers: Institutional strategies for improving rates. *N C Med J* 2004;65(6):323-9.
30. Johnson JG, Talbot TR. New approaches for influenza vaccination of healthcare workers. *Curr Opin Infect Dis* 2011;24(4):363-9.
<https://doi.org/10.1097/QCO.0b013e328347b0e7>.
31. Rothan-Tondeur M, de Waizieres B, Lejeune B, Gavazzi G. Influenza vaccine coverage for healthcare workers in geriatric setting in France. *Aging Clin Exp Res* 2006;18(6):512-6.
<https://doi.org/10.1007/BF03324852>.
32. Kramarz P, Ciancio B, Nicoll A. Seasonal and pandemic influenza vaccines for elderly and other risk groups: A review of available data. *Pol Arch Med Wewn* 2009;119(10):654-9.
33. Contal E, Putot A, Dipanda M, Perrin S, Akgassou S, Sordet-Guepet H, et al. The seasonal flu vaccination among caregivers in geriatric units: Up-to-date. [Article in French]. *Rev Epidemiol Santa Publique* 2016;64(6):415-423.
DOI: 10.1016/j.respe.2016.06.333.
34. Hofmann F, Ferracin C, Marsh G, Dumas R. Influenza vaccination of healthcare workers: A literature review of attitudes and beliefs. *Infection* 2006;34(3):142-7.
<https://doi.org/10.1007/s15010-006-5109-5>.
35. Rehmani R, Memon JI. Knowledge, attitudes and beliefs regarding influenza vaccination among healthcare workers in a Saudi hospital. *Vaccine* 2010;28(26):4283-7.
<https://doi.org/10.1016/j.vaccine.2010.04.031>.